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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,387	08/14/2007	Joel M. Friedman	96700/1175	8882

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EXAMINER	
CARLSON, KAREN C	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,387	FRIEDMAN ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-14 and 45-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-9,11-14 and 45-54* is/are rejected.

7)☐ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2006, 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group 2, Claims 6-14 and 45-54, in the reply filed on March 26, 2009 is acknowledged.

Claims 1-5 and 15-44 have been cancelled. Claims 6-14 and 45-54 are currently pending and are under examination.

Benefit of priority is to April 21, 2004.

The disclosure is objected to because of the following informalities:

At page 8 of the specification, the Ray et al. citation is incorrect. The citation is at 124(25).

Appropriate correction is required.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 11-14, and 50-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Ajisaka et al. (1983; USP 4,377,512).

Ajisaka et al. teach a solution comprising inulin and hemoglobin and subjecting the solution to lyophilization (Example 1 at Col. 2, lines 56-62) or washed with acetone and subjected to air drying (Example 2 at Col. 3, line 32). The hemoglobin was oxygenated because Ajisaka et al. teach that it is an oxygen carrier (Col. 1, lines 20-35 and Table 3).The in vivo half-residence times of inulin-hemoglobin is longer than that of hemoglobin alone (Example 5 and Table 3).

Therefore, Ajisaka et al. teach a method for preparing a powdered protein by mixing the protein with inulin and drying the mixture **(Claim 6)** by lyophilization **(Claim 11)** or by air drying **(Claim 12)**. It takes heat to evaporate a liquid; hence, all solutions cool upon drying. Since acetone in the solution will lower the vapor pressure of the solution, it will evaporate more rapidly than if the acetone was not present **(Claim 13)**. The protein used in the method was hemoglobin **(Claim 14)** which was oxygenated **(Claim 50)**. Because the method claimed and the method taught in Ajisaka et al. are the same, and the half residence times of inulin-hemoglobin was shown by Ajisaka et al. to be longer than that of hemoglobin itself, it is concluded that the oxygenated hemoglobin was resistant to oxidation **(Claim 51)**, stable at room temperature **(Claim 52)**, and comprised less than 20% **(Claim 53)** or less than 10% **(Claim 54)** met-hemoglobin.

Claims 6 and 8-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Oliver et al. (June 5, 2003; WO 03/045163).

Oliver et al. claim a method for preparing a sugar-protein conjugate comprising a proteinaceous foodstuff (Oliver Claim 1a) and one or more oligosaccharide sugars including inulin (Oliver Claim 1b and 4), and one or more monosaccharides including glucose (Oliver Claim 1c and 2) and preparing the sugar-protein as a dry material (Oliver Claim 14) which is defined in the specification (page 10, para. 1 and 2) as evaporation/air-drying and freeze-drying (which is lyophilization).

Therefore, Oliver et al. teach a method for preparing a powdered protein by mixing a protein with inulin and drying the mixture (**Claim 6**), wherein the mixture comprises protein, inulin, and a reducing sugar (**Claim 8**) such as glucose (**Claim 9**), wherein the mixture is lyophilized (**Claim 11**) or air-dried (**Claim 12**). It takes heat to evaporate a liquid; hence, all solutions cool upon drying (**Claim 13**).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-9, 11, 14, and 45-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Privalle et al. (issued June 8, 2004 and having priority to at least August 16, 2001; USP 6,747,132).

Privalle et al. teach that bifunctional conjugates useful for conjugating/stabilizing hemoglobin are include inulin and PEG (Col. 9, lines 64-65 and Col. 10, lines 48-49). At Col. 12, lines 59-65, Privalle et al. teach that the modified hemoglobin can be freeze-

dried (which is lyophilization) and that monosaccharides such as glucose are used during lyophilization as effective stabilizing agents.

It would have been obvious for a person having ordinary skill in the art to lyophilize (**Claim 6, 11)** a mixture of PEG-hemoglobin (**Claim 14, 45-49**), inulin, and a reducing sugar (**Claim 8**) such as glucose (**Claim 9**) because Privalle et al. teach that conjugating hemoglobin to PEG and/or inulin stabilizes hemoglobin and glucose is an effective stabilizing agent used during lyophilization of proteins. **Claim 7** is included in this rejection because the use of inulin derived from chickory root appears to be an obvious design choice and the specification does not point out the superiority of inulin derived from chickory root over other plant materials. Claims 46 to 54 are included in the rejection because the method rendered obvious by the teachings of Privalle et al. would be expected to render hemoglobins comprising at least 2 PEGs (**Claims 46-49**) and/or an oxygenated hemoglobin (**Claim 50**) that is resistant to oxidtation (**Claim 51**), stable at room temperature (**Claim 52**), and has less than 20% (**Claim 53**) or less than 10% (**Claim 54**) met-hemoglobin.

Claims 6- 9, 11, 14, and 45-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Heller et al. (1999; Conformational stability of lyophilized PEGylated proteins in a phase-separating system. J. Pharmaceutical Sciences. 88(1): 58-64) and Privalle et al. (issued June 8, 2004 and having priority to at least August 16, 2001; USP 6,747,132).

Heller et al. teach that PEGylated hemoglobin (Claims **14, 45-47**) is more stable when lyophilized (**Claim 11**) in PEG/dextran formulations (see abstract, page 58 right col., para. 3; page 60, right col., para. 1) and that dextran can form protective glasses. The hemoglobins comprised two PEGs (page 60, left col., line 9; **Claims 48, 49).** The PEG-hemoglobin was lyophilized in PEG/dextran and hemoglobin retained it's structure over hemoglobin alone (page 60, right col., para. 1).

Heller et al. do not teach to substitute dextran for inulin or to add a reducing sugar such as glucose to the solution.

Privalle et al. teach that bifunctional conjugates useful for conjugating/stabilizing hemoglobin are dextran, inulin, and PEG (Col. 9, lines 64-65 and Col. 10, lines 48-49). At Col. 12, lines 59-65, Privalle et al. teach that monosaccharides such as glucose are used during lyophilization as effective stabilizing agents.

It would have been obvious for a person having ordinary skill in the art to substitute dextran in the PEG/dextran formulations taught in Heller et al. with the inulin equivalent taught in Privalle et al. because Heller et al. teach that dextran forms protective glasses with hemoglobin and Privalle et al. teach that dextran and inulin are functional equivalents used to stabilize hemogloblin (**Claim 6**). It would have been obvious to a person having ordinary skill in the art to add a reducing sugar (**Claim 8**) such as glucose (**Claim 9**) to the PEG/Inulin solution used in the phyophilization of PEG-hemoglobin because Privalle et al. teach that glucuse is an effective stabilizing agent of proteins undergoing lyophilization. **Claim 7** is included in this rejection because the use of inulin derived from chickory root appears to be an obvious design choice and

the specification does not point out the superiority of inulin derived from chickory root over other plant materials.

Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

It is noted that tagatose is an artificial sweetener. The Examiner does not find tagatose used in the manner claimed, that is, to prepare powdered proteins, or references teaching the functional equivalents of tagatose to glucose, and in particular not in the preparation of powdered proteins.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson whose telephone number is 571-272-0946. The examiner can normally be reached on 6:00 AM - 4:00 PM, Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen Cochrane Carlson/
Primary Examiner, Art Unit 1656